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Fate of famoxadone in the environment

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Abstract: The fate of famoxadone [Famoxate®, 3-anilino-5-methyl-5-(4-phenoxyphenyl)-1,3-oxazolidine-2,4-dione] in the aquatic and soil environment was examined. It was found to be relatively stable at pH 5, but hydrolysed rapidly in pH 7 and 9 buffer solutions. Primary hydrolytic degradation reactions included the opening of the oxazolidinedione ring and the cleavage of the oxazolidinedione-aminophenyl linkage. The compound degraded rapidly in soil by both hydrolytic and microbial action. In addition to the generation of [^{14}C] carbon dioxide and unextractable bound residues, hydroxylation and hydrolysis reactions occurred to yield multiple degradation products. Nitration of famoxadone at the 2- or 4-phenylamino position was observed as a novel non-biological degradation reaction of famoxadone in soil. Degradation in aqueous solution (pH 5) and on soil surfaces was accelerated under simulated sunlight irradiation. Famoxadone exhibited negligible soil mobility potential, and its primary degradation products were also shown to dissipate rapidly in the environment.

Keywords: famoxadone; hydrolysis; photolysis; soil; degradation

1 INTRODUCTION

Famoxadone [Famoxate®, DPX-JE874, 3-anilino-5-methyl-5-(4-phenoxyphenyl)-1,3-oxazolidine-2,4-dione; Fig 1,] is a novel fungicide being developed by DuPont Agricultural Products for the preventive control of a broad spectrum of fungal pathogens such as *Plasmopara viticola* Berl & de Toni (grape downy mildew), *Phytophthora infestans* (Mont) de Bary (potato/tomato late blight), *Pseudoperonospora cubensis* Rostow (cucumber downy mildew), *Septoria tritici* Rob (wheat leaf blotch), S *nodorum* Berk (wheat glume blotch) and *Alternaria solani* Sorauer (potato/tomato early blight). Excellent activity has been also observed against other Ascomycetes, as well as against pathogens within the *Pucciniaceae* family of the Basidiomycete class. Famoxadone has a novel mode of action in that it inhibits electron transport in oxidative phosphorylation in the fungal mitochondria and energy production.[1] It is highly active against spore germination and mycelial growth.[2] This summary describes the fate of famoxadone in water and soil test systems. Studies were conducted using famoxadone labeled in the phenoxyphenyl and in the phenylamino ring, abbreviated as [POP-^{14}C]- and [PA-^{14}C]famoxadone respectively (Fig 1).

2 EXPERIMENTAL AND RESULTS

2.1 Degradation in the aquatic environment

Famoxadone, with low water solubility (52 μg litre^{-1}), is relatively stable to hydrolytic degradation under dark conditions in pH5 buffer solution (half-life, DT_{50}:41 days) but hydrolyses rapidly in pH 7 and 9 buffer solutions at 25 °C (DT_{50} 2 days and <2 h, respectively). Primary hydrolytic degradation reactions include the opening of the oxazolidinedione ring *via* attack on either of the carbonyl moieties by hydroxide ion to yield compounds **2** and **3** (Fig 2), and the cleavage of the oxazolidinedione-aminophenyl linkage to yield various products from both the phenoxyphenyl (compounds **4** and **5**) and the aminophenyl moieties [benzene (**7**), catechol (**8**) and phenol (**9**)]. Famoxadone and its degradation products dissipate rapidly in the aqueous sediment system (DT_{50} < 1 day, DT_{90} 14 days). Significant impact or persistence in the aquatic environment is not anticipated. The hydrolysis pathway of famoxadone is presented in Fig 2.

Direct aqueous photolysis is not significant at pH 7; however, the degradation rate in acidic buffer solution (pH 5) is accelerated under simulated sunlight irradiation (DT_{50} 4.6 *vs* 41 days) to yield compounds **3, 4, 5, 8, 9** and **10**. Ring opening and cleavage of the oxazolidinedione-aminophenyl linkages are the primary reactions observed. Based on results from photodegradation studies with the parent and major degradation products compounds (**3, 4** and **10**), the profused aqueous photodegradation degradation pathway of famoxadone is presented in Fig 3.

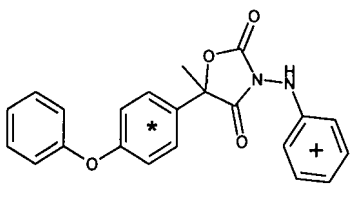

Figure 1. Structure of famoxadone. + Denotes [PA-^{14}C] famoxadone. *Denotes [POP-^{14}C] famoxadone.

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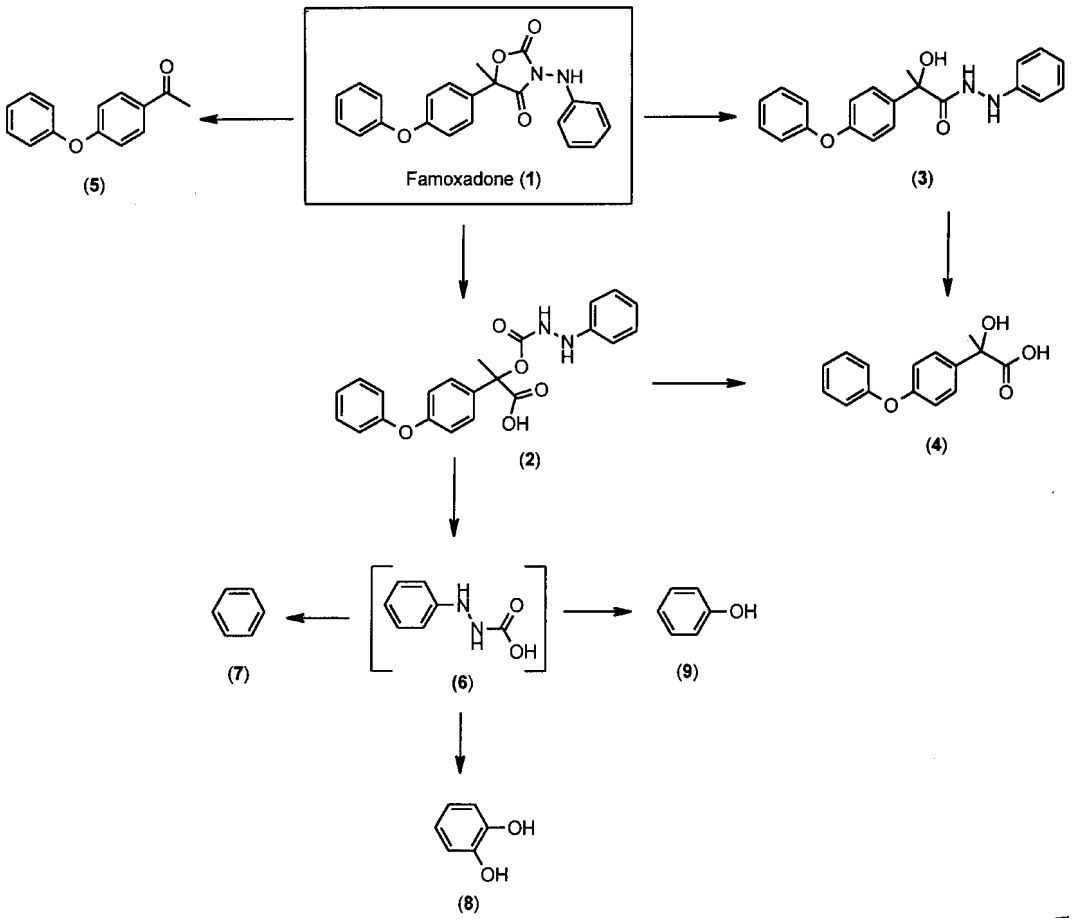

Figure 2. Primary hydrolytic degradation reactions of famoxadone.

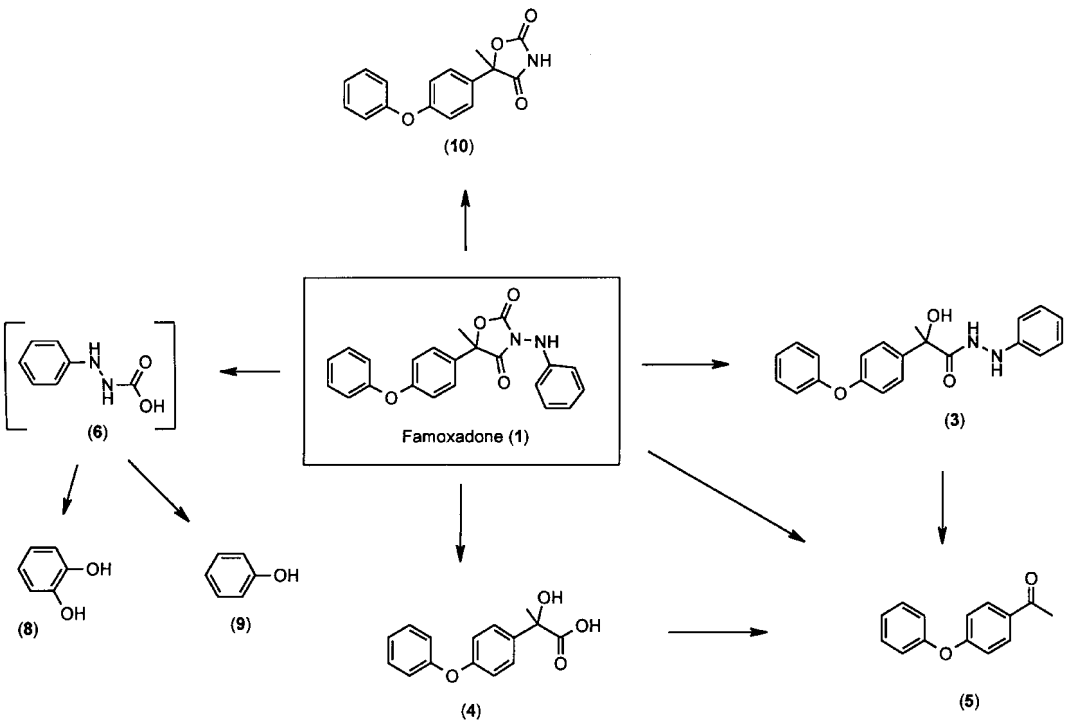

Figure 3. Proposed photodegradation pathway for famoxadone.

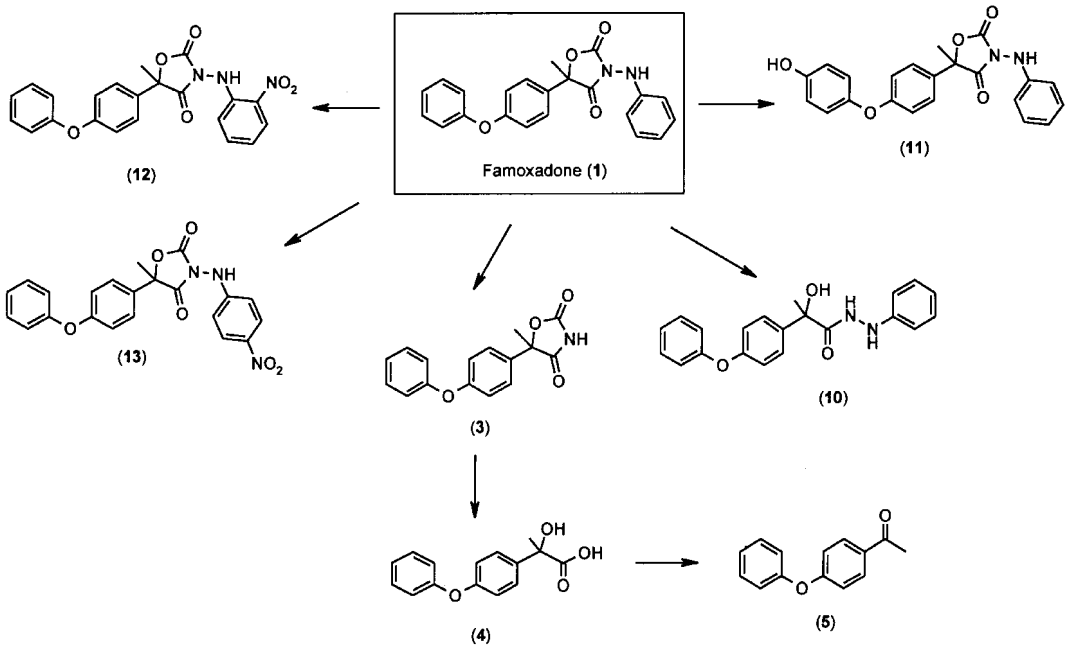

Figure 4. Pathway for primary degradation of famoxadone in soil.

2.2 Fate in the soil environment

Famoxadone degrades rapidly in the soil under laboratory aerobic and anaerobic incubation conditions (DT_{50} 6 and 28 days, respectively), mainly by both hydrolytic and microbial action. [^{14}C] carbon dioxide and unextractable bound residues are recovered as primary terminal residues. The DT_{50} of famoxadone in an aerobic aqueous sediment metabolism study is <1 day. The major degradation pathways include the hydroxylation of the parent molecule at the 4′-phenoxyphenyl position to yield compound **11** (Fig 4) and the hydrolytic cleavage of the oxazolidinedione-aminophenyl linkage to yield compounds **3, 4** and **5**. A novel nitration reaction (at the 2- or 4-phenylamino position) in soil yields the nitro-analogs of famoxadone (**12** and **13**). The soil degradation rate is accelerated when famoxadone is exposed to simulated sunlight (DT_{50} 12 *vs* 28 days). The soil adsorption coefficient of famoxadone (K_{oc}) is 3740. Aged soil column leaching studies show famoxadone and its soil metabolites to be compounds with low soil mobility potential. Significant movement and persistence of famoxadone in the soil environment is not anticipated. The primary soil degradation pathway of famoxadone is presented in Fig 4.

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Comparative metabolism of famoxadone in fish, plants and animals

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Abstract: The fate and comparative metabolism of famoxadone in fish, plants and animals were evaluated. Famoxadone residues were retained by the fish after exposure (BCF 2800), mainly in the viscera; however, rapid and complete elimination/depuration of the absorbed residues occurred within seven days after the exposed fish were placed in untreated water. Minimal absorption, translocation, and metabolism of famoxadone were observed in grape and potato plants after foliar treatment. Metabolism of famoxadone in the wheat plants, rats, goats, and poultry was extensive. Transfer of ^{14}C-residues to the wheat grain, milk, eggs, organs and tissues was minimal. Common metabolic reactions of famoxadone in plants and animals include aryl hydroxylation, cleavage of the anilino-oxazolidinedione and phenoxy-phenyl ether linkages, opening of the oxazolidinedione ring and conjugation.

Keywords: famoxadone; metabolism; bioconcentration; fish; plant; rat; goat; chicken

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